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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,914	WEINSTEIN, DAVID E.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cov r she t with th correspondence address --

P riod for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0802* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The following documents and materials have been entered:

a) the Reply to Restriction Requirement filed March 24, 2003;

b) the Associate Power of Attorney and Change of Address filed September 9, 2003;

c) the Amendment filed September 17, 2003; and

d) the paper and computer readable forms of the Sequence Listing, and Statement under 35 CFR 1.821(f), filed September 17, 2003.

Election/Restriction

2. Applicant's election without traverse of Group I, claims 31-43, 49-56, and 62-64 in the Reply filed March 24, 2003 is acknowledged. It is noted that while Applicant has stated in the Reply that the election is "without traverse," a traversal of the restriction requirement was included in Applicant's reply. Upon consideration of Applicant's arguments and further consideration of the field of search required to examine Groups I and II, the restriction requirement is withdrawn. Groups I and II, claims 31-64, have been examined.

Specification

3. The title of the invention is not descriptive of the subject matter now claimed. A new title is required that is clearly indicative of the invention to which the claims are directed.

4. The use of the trademarks PERCOLL, FUNGIZONE, LAB-TEK, and VECTASTAIN have been noted in this application. The trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 31-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make

or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Claim 31 and claims dependent therefrom are drawn to methods "for determining whether a subject has an astrocytoma" comprising a step of "assaying for CD81 expression in a diagnostic sample of cells of astrocytic lineage of the subject, wherein no detection of expression of CD81 in cells of astrocytic lineage of the subject is diagnostic of an astrocytoma." Claim 33 and claims dependent therefrom are drawn to methods "for assessing the efficacy of astrocytoma therapy in a subject who has undergone or is undergoing treatment for an astrocytoma" comprising a step of "assaying for CD81 expression in a diagnostic sample of cells of astrocytic tumor cells of the subject, wherein no detection of expression of CD81 in astrocytic tumor cells of the subject is indicative of unsuccessful astrocytoma therapy."

The specification provides evidence that CD81 is expressed on the surface of cultured astrocytes, but not expressed on the surface of the rat astroglial cell line C6 (see pages 39-40). Further, Applicant demonstrates that CD81 mRNA is expressed in astrocytes, but not expressed in various rat, mouse, and human astrocytoma cells lines, and states that "the present data suggest that CD81 may play a role in astrocyte tumor progression" (see page 44 and Figure 6). While the data provided in the specification do establish that various astrocytic cell lines fail to express CD81, the instant claims are drawn to methods in which astrocytic cells from a subject are assayed, and in which the absence of CD81 expression in such cells is indicative of an astrocytoma or of failed astrocytoma therapy. Accordingly, enablement of the claimed invention requires that an

association exist between astrocytomas and the absence of CD81 expression in astrocytic cells obtained from a subject. The instant specification does not provide evidence of such an association. While the specification provides evidence that CD81 expression is absent in some astrocytoma cell lines, it is well known to those of skill in the art that cultured cell lines typically exhibit different expression patterns than primary cells, which patterns result from, e.g., attenuating mutations associated with adaptation of cells for growth in culture. Thus, a molecule that is expressed or not expressed in a cell line may or may not exhibit the same pattern in primary cells. Further, the prior art as exemplified by Guha et al (Oncogene 15:2755-2765 [1997]) teaches that such differences in expression patterns are in fact seen in astrocytoma cells lines as compared to actual tumors, citing truncated EGFR as an example of a protein that is expressed in astrocytomas but not in astrocytoma cell lines (see page 2755, right column). Accordingly, absent evidence that CD81 expression is actually absent in astrocytoma cells, it is unpredictable as to whether the lack of CD81 expression observed by Applicant in cultured cells also occurs in primary tumor cells, and therefore as to whether there is or is not an association between astrocytomas and CD81 expression in a subject. Lacking guidance from the specification, one of skill in the art may look to the teachings of the art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to any association or correlation between CD81 expression in astrocytic cells from a subject and astrocytomas. Given the high skill level of one skilled in the relevant art, it is clearly within the ability of such an artisan to conduct further experimentation directed at

determining whether such a correlation or association exists. However, the outcome of such further research cannot predicted, and it is unknown as to whether any quantity of experimentation would actually result in the identification of an association between CD81 expression in a subject and astrocytomas. Thus, it would clearly require undue experimentation to use the claimed invention. With further regard to claim 33 and claims dependent therefrom, it is also noted that neither the specification nor the prior art provide any evidence that any type of astrocytoma therapy administered to a subject, whether successful or unsuccessful, alters CD81 expression in astrocytic tumor cells of the subject. While experimentation could also be conducted to determine whether successful astrocytoma therapy does affect CD81 expression, it is unpredictable as to what the outcome of such experimentation might be, and as to whether any quantity of experimentation would be sufficient to identify such a relationship. Accordingly, the quantity of experimentation required to practice the methods of claim 33 and claims dependent therefrom is also undue.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 31-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31, 32, and 35-51 are indefinite over the recitation of the term "diagnostic sample of cells of astrocytic lineage." Neither the specification nor the prior art provides a clear definition of this language, and it is unclear as to whether any "sample of cells of

astrocytic lineage" could be considered to be "diagnostic" and thereby meet the requirements of the claims, or whether the use of the term "diagnostic" is further limiting. To the extent that the term "diagnostic" may be further limiting, it is also unclear as to what features or properties of a sample would render it "diagnostic." Clarification is required.

Claims 32, 48, and 51 are indefinite over the recitation of the language "wherein the diagnostic sample of cells of astrocytic lineage of the subject is assayed *in vitro*." This recitation does not make clear whether the claims are further limiting of the assaying step of claim 31 (such that the previously recited "assaying for CD81 expression" is to be performed *in vitro*), or whether the claims merely require that the diagnostic sample be further subject to any kind of *in vitro* assay.

Claims 33-34 and 52-64 are indefinite over the recitation of the term "diagnostic sample of cells of astrocytic tumor cells." First, neither the specification nor the prior art provides a clear definition of this language, and it is unclear as to whether any "sample of cells" could be considered to be "diagnostic" and thereby meet the requirements of the claims, or whether the use of the term "diagnostic" is further limiting. To the extent that the term "diagnostic" may be further limiting, it is further unclear as to what features or properties of a sample would render it "diagnostic." Second, regarding the recitation "diagnostic sample of cells of astrocytic tumor cells," it is unclear as to whether this language is merely referring to a "diagnostic" sample of cells that are astrocytic tumor cells, or whether this language indicates that a "diagnostic sample" is obtained from

amongst, e.g., a population of astrocytic tumor cells (i.e., that only a subset of astrocytic tumor cells would be considered "diagnostic" cells). Clarification is required.

Claims 34, 61, and 64 are indefinite over the recitation of the language "wherein the diagnostic sample of cells of astrocytic lineage of the subject is assayed *in vitro*." First, there is insufficient antecedent basis for the limitation "the diagnostic sample of cells of astrocytic lineage." Second, this recitation does not make clear whether the claims are further limiting of the assaying step of claim 33 (such that the previously recited "assaying for CD81 expression" is to be performed *in vitro*), or whether the claims merely require that the diagnostic sample be further subject to any kind of *in vitro* assay.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-1234.

Diana B. Johannsen
Patent Examiner
January 23, 2004